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10/555,865	08/25/2006	Manuel Sarasa Barrio	105090.61194US	6865

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EXAMINER	
BALLARD, KIMBERLY	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
07/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,865	SARASA BARRIO, MANUEL	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5 and 8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 4, 6 and 7 have been amended as requested in the response filed March 29, 2010. Following the amendment, claims 1-19 are pending in the present application.

2. Claims 5 and 8-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 4, 2009.

3. Claims **1-4** and **6-7**, drawn to the extent of the peptides of SEQ ID NO: 2 and SEQ ID NO: 3 for use in the claimed method, are under examination in the current office action.

Withdrawn Objections

4. The objections to claims 4, 6 and 7 are withdrawn in view of Applicant's amendments to the claims.

Maintained Rejections

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for the treatment of a disease characterized by the abnormal accumulation of amyloid deposits in the brain of a patient, comprising administering to a patient in need thereof an effective amount of an amyloid β peptide conjugated to a protein immunogen for the production of antibodies that specifically recognize any of the predominant variants of Aβ40 or Aβ42 peptide, wherein the Aβ peptide is SEQ ID NO: 2, SEQ ID NO: 3, a peptide comprising at least 5 contiguous amino acid residues of SEQ ID NO: 2 or 3, or a peptide resulting from lengthening by addition of linker amino acid residues appropriate for conjugating the protein to the peptide of SEQ ID NO: 2 or SEQ ID NO: 3,

does not reasonably provide enablement for a method for the prevention of a disease characterized by amyloid deposits in the brain as broadly claimed or for the therapeutic method comprising the administration of any Aβ peptide fragment resulting from shortening by elimination of amino acids of the N-terminal and/or C-terminal ends of SEQ ID NO: 2 or SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

7. In the response filed March 29, 2010, Applicant points to MPEP 2164.02 and asserts that animal models are routinely used in the art for preclinical testing of drugs, and such results are then extrapolated to clinical efficacy in humans. Applicant attests that the animal models selected were not arbitrary, but rather art-accepted animal models, and proved Sarasa & Pesinin (*Curr Alzheimer Res*. 2009; 6: 171-178) as evidence that several animal models develop amyloid deposits in a very similar fashion to humans. Further, Applicant notes that the use of humans for preclinical testing would be unrealistic and unethical. Applicant argues that the side effects noted in the clinical trial of another method of treatment using different peptides are not relevant to the claimed methods and do not render the present disclosure insufficient. Rather, the results of that clinical trial as assessed years later (evidenced by Applicant in Vellas et al., *Curr. Alzheimer Res*. 2009; 6:144-151) corroborates the vaccination properties shown by the peptides in the animal model. Thus, the fact that a specific peptide may produce side effects in some patients, Applicant argues, does not deny the fact that the peptide really works *in vivo*.

With respect to the peptide fragment length, Applicant asserts that one of skill in the art interpreting the claims within the context of the invention and appreciating that the sequences must retain good activity could find active variants by modifying the length of SEQ ID NO: 2 (Aβ 33-40) and SEQ ID NO: 3 (Aβ 33-42), without resorting to undue experimentation.

8. Applicant's arguments submitted March 29, 2010 have been fully considered but they are not persuasive. In the first instance, the examiner does not contest that animal models, and even *in vitro* models, are necessary and reasonable for the development of therapeutics in humans. The examiner also does not contest that there are many suitable animal models for studying Alzheimer's disease or other amyloid-related diseases, and even cited relevant art indicating that the PDAPP transgenic mouse is an art-accepted model for the study of Alzheimer's disease. Additionally, the animals used in the instant disclosure are perfectly suitable for developing peptide vaccine compositions. Indeed, the validity of appropriate animal models in the present application or other studies concerning the development of Aβ vaccines was never challenged. Instead, the purpose for citing the animal and human clinical studies was to illustrate the complexity and unpredictability in the art; even with the most solid of evidence in animal studies, there can be unexpected outcomes when bench science is translated to clinical use in human patients.

And while the presently disclosed animal model involving rabbits is appropriate, for example, for the development of antibodies or even for evaluating antibody responses to various immunogenic peptide vaccines, it is not suitable for studying the preventative effects of the elicited antibody response, such as for the prevention of a disease characterized by the accumulation of amyloid deposits in the brain as claimed, particularly since the rabbits used were presumably healthy and not displaying brain pathology consist with an amyloid-related disease. In other words, the evidence and guidance presented in the instant specification are not commensurate in scope with the

presently claimed invention which broadly encompasses the *prevention* of any disease characterized by the accumulation of brain amyloid deposits. As noted in the previous office action, the relevant art indicates that diseases such as Alzheimer's disease, cerebral amyloid angiopathy, and Down's syndrome, for instance, which all fall within the scope of the present invention, are not preventable. Coupled with the fact that the claims encompass the use of peptide fragments which may be too short to generate an appropriate, therapeutically effective antibody response, the complexity and unpredictability in the relevant art, and the lack of evidence or working examples directed to a preventative effect of the claimed method, undue experimentation would be required of the skilled artisan to practice the present invention in its full scope. Accordingly, the rejection of claims 1-4, 6 and 7 is maintained. It is noted that deletion of the words "prevention and/or" from the claims, along with deletion of reference to the use of truncated peptides of SEQ ID NOs: 2 and 3, would overcome this rejection.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/72880 A2 by Schenk et al. (published December 7, 2000; reference AM on IDS filed 11/07/2005). The rejection is maintained for reasons of record and as discussed below.

11. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2006/0188512 A1 by Yednock et al. (published August 24, 2006; priority to February 1, 2003). The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

12. Because Applicant has formulated concurrent arguments for both the Schenk et al. reference and the Yednock et al. reference, these rejections will be addressed together. In the response filed March 29, 2010, Applicant argues that both the Schenk reference and the Yednock reference teach away from the present invention. For example, Applicant notes that Schenk teaches that "fragments from the N-terminal half of Aβ are preferred", and that Yednock states that "fragment Aβ15-24 and subfragments of 7-9 contiguous amino acids thereof are preferred." Applicant asserts that the use of SEQ ID NO: 2 in the present invention was not a random selection, but rather a purposeful selection in that it possesses the ability of decreasing levels of Aβ pepide in an exceptional way, contrary to the expectations in the art. Therefore, Applicant argues, Schenk and Yednock fail to teach the ability of SEQ ID NO: 3 or SEQ ID NO: 2 to reduce the accumulation of amyloid peptide or the use of these sequences as immunogens.

13. Applicant's arguments have been fully considered but they are not persuasive. While the Schenk and Yednock references may state preferred Aβ peptides for use in the therapeutic vaccines, they also clearly teach the C-terminal Aβ peptides presently claimed. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied,* 493 U.S. 975 (1989). See also >*Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005). Accordingly, it does not matter whether or not the C-terminal Aβ peptides are preferred embodiments or not, because these C-terminal peptides are taught by both Schenk and Yednock to be useful in the treatment of diseases associated with amyloid deposits in the brain, such as Alzheimer's disease, and thus are anticipatory for the instantly recited invention. Further, concepts related to “unexpected results” as asserted by Applicant are not applicable in a rejection based upon anticipation – such concepts find relevance only under rejections based upon obviousness. As such, the rejection of claims 1-4, 6 and 7, as being anticipated by Schenk et al. and by Yednock et al. are maintained.

Conclusion

14. No claims are allowed.

15. This application contains claims 5 and 8-19 drawn to an invention nonelected with traverse in the reply filed on September 4, 2009. A complete reply to the final

rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard
Art Unit 1649

/Daniel E Kolker/
Primary Examiner, Art Unit 1649
July 6, 2010